SUGGESTED GROUPINGS OF U.S. FDA-APPROVED ANTIMICROBIAL AGENTS THAT SHOULD BE CONSIDERED FOR ROUTINE TESTING AND REPORTING ON FASTIDIOUS ORGANISMS BY CLINICAL MICROBIOLOGY LABORATORIES

FOR USE WITH CLSI DOCUMENT M2 – DISK DIFFUSION

	***Haemophilus* spp.**[e]	***Neisseria gonorrhoeae*[i]**	***Streptococcus pneumoniae*[j]**	***Streptococcus* spp. Beta-hemolytic group**[r]	***Streptococcus* spp. Viridans group**[r]
GROUP A PRIMARY TEST AND REPORT	Ampicillin[e,g]		Erythromycin[a,n]	Clindamycin[n,q] Erythromycin[a,n,q]	
	Trimethoprim - sulfamethoxazole		Penicillin (oxacillin disk)[k]		
			Trimethoprim-sulfamethoxazole	Penicillin[o] or ampicillin	
GROUP B[b] PRIMARY TEST REPORT SELECTIVELY	Ampicillin-sulbactam		Clindamycin[n]	Cefepime or cefotaxime or ceftriaxone	Cefepime Cefotaxime Ceftriaxone
	Cefotaxime[e] or ceftazidime[e] or ceftriaxone[e]		Gemifloxacin[j] Levofloxacin[j] Moxifloxacin[j] Ofloxacin		
	Cefuroxime (parenteral)		Telithromycin		
	Chloramphenicol[e,n]		Tetracycline[d]		
	Meropenem[e,h]		Vancomycin[k]	Vancomycin	Vancomycin
GROUP C[c] SUPPLEMENTAL REPORT SELECTIVELY	Azithromycin[f] Clarithromycin[f]	Cefixime or cefpodoxime	Chloramphenicol[n]	Chloramphenicol[n]	Chloramphenicol[n]
	Aztreonam	Cefotaxime or ceftriaxone	Linezolid		Clindamycin[n]
	Amoxicillin-clavulanic acid[f]				
	Cefaclor[f] Cefprozil[f]	Cefoxitin Cefuroxime	Rifampin[l]	Levofloxacin[n] Ofloxacin[n]	Erythromycin[a,n]
	Cefdinir[f] or cefixime[f] or cefpodoxime[f]	Ciprofloxacin or ofloxacin		Linezolid	
	Cefuroxime (oral)			Quinupristin-dalfopristin[p]	
	Ciprofloxacin or levofloxacin or lomefloxacin or moxifloxacin or ofloxacin Gemifloxacin	Penicillin[i]			
	Ertapenem or imipenem	Spectinomycin			Linezolid
	Rifampin	Tetracycline			
	Telithromycin[f]				
	Tetracycline[d]				

"Warning": The following antimicrobial agents should not be routinely reported for bacteria isolated from the CSF and which are included in this document. These antimicrobial agents are not the the drugs of choice and may not be effective for treating CSF infections caused by these organisms (i.e., the bacteria included in Tables 2A to 2L in CLSI M100):

- agents administered by oral route only
- first- and second-generation cephalosporins (except cefuroxime parenteral)
- clindamycin
- macrolides
- tetracyclines
- fluoroquinolones

NOTE 1: Selection of the most appropriate antimicrobial agents to test and to report is a decision made best by each clinical laboratory in consultation with the infectious disease practitioners and the pharmacy, as well as the pharmacy and therapeutics and infection control committees of the medical staff. The lists for each organism group comprise agents of proven efficacy that show acceptable *in vitro* test performance. Considerations in the assignment agents to Groups A, B, and, C include clinical efficacy, prevalence of resistance, minimizing emergence of resistance, cost, FDA clinical indications for usage, and current consensus recommendations for first-choice and alternative drugs, in addition to the specific comments in footnotes "b" and "c". Unexpected resistance should be reported (eg, resistance of Enterobacteriaceae to carbapenems). Tests on selected agents may be useful for infection-control purposes.

NOTE 2: The listing of drugs together in a single box designates clusters of agents for which interpretive results (susceptible, intermediate, or resistant) and clinical efficacy are similar. Within each box, an "or" between agents designates those agents for which cross-resistance and cross-susceptibility are nearly complete. This means combined major and very major errors are fewer than 3% and minor errors are fewer than 10%, based on a large population of bacteria tested. In addition, to qualify for an "or", at least 100 strains with resistance to the agents in question must be tested and a result of "resistant" must be obtained with all agents for at least 95% of the strains. "Or" is also used for comparable antimicrobial agents when tested against organisms for which "susceptible-only" interpretive criteria are provided (eg, cefotaxime or ceftriaxone with *Haemophilus influenzae*). Thus, results from one agent connected by an "or" could be used to predict results for the other agent. **For example,** a non-ESBL-producing isolate of Enterobacteriaceae susceptible to cefotaxime can be considered susceptible to ceftriaxone. **The results obtained from testing cefotaxime would be reported and a comment could be included on the report that the isolate is also susceptible to ceftriaxone. When no "or" connects agents within a box, testing of one agent cannot be used to predict results for another either owing to discrepancies of insufficient data.**

NOTE 3: Information in boldface type is considered tentative for one year.

Footnotes

General Comments

a. Susceptibility and resistance to azithromycin, clarithromycin, and dirithromycin can be predicted by testing erythromycin.

b. Group B represents agents that may warrant primary testing but which should be reported only selectively, such as when the organism is resistant to agents of the same class in Group A. Other indications for reporting the result might include selected specimen sources (e.g. third-generation cephalosporin for isolates of *H. influenzae* from cerebrospinal fluids or CSF); stated allergy or intolerance, or failure to respond to an agent in Group A; polymicrobial infections; infections involving multiple sites with different microorganisms; or reports to infection control as an epidemiologic aid.

c. Group C represents alternative or supplemental antimicrobial agents that may require testing in those situations that harbor endemic or epidemic strains resistant to one or more of the primary drugs (especially in the same class, e.g. beta-lactams), or for the treatment of unusual organisms, or reporting to infection control as an epidemiologic aid.

d. Organisms that are susceptible to tetracycline are also considered susceptible to doxycycline and minocycline.

Haemophilus spp.

e. Only results of testing with ampicillin, one of the third-generation cephalosporins, chloramphenicol, and meropenem should be reported routinely with cerebrospinal fluid isolates of *Haemophilus influenzae*.

f. Amoxicillin/clavulanic acid, azithromycin, clarithromycin, lorcarbef, cefdinir, cefixime, cefpodoxime, cefuroxime and telithromycin are oral agents that may be used as empiric therapy for respiratory tract infections due to *Haemophilus* spp. The results of susceptibility tests with these antimicrobial agents are often not useful for management of individual patients. However, susceptibility testing of *Haemophilus* spp. with these compounds may be appropriate for surveillance or epidemiologic studies.

g. The results of ampicillin susceptibility tests should be used to predict the activity of amoxicillin. The majority of isolates of *H. influenzae* that are resistant to ampicillin and amoxicillin produce a TEM-type-beta-lactamase. In most cases a direct beta-lactamase test can provide a rapid means of detecting ampicillin and amoxicillin resistance.

h. Clinical indications and relevant pathogens include bacterial meningitis and concurrent bacteremia in association with meningitis caused by *Haemophilus influenzae* (beta-lactamase and non-beta-lactamase producing strains).

Neisseria gonorrhoeae

i. A beta-lactamase test will detect one form of penicillin resistance in *N. gonorrhoeae* and also may be used to provide epidemiologic information. Strains with chromosomally mediated resistance can be detected only by additional susceptibility testing, such as the disk diffusion method or the agar dilution MIC method.

Streptococcus pneumoniae

j. ***S. pneumoniae* isolates susceptible to levofloxacin are predictably susceptible to gemifloxacin and moxifloxacin. However, *S. pneumoniae* susceptible to gemifloxacin or moxifloxacin cannot be assumed to be susceptible to levofloxacin.**

k. Penicillin and cefotaxime or ceftriaxone or meropenem should be tested by a reliable MIC method (such as that described in CLSI document M7) and reported routinely with CSF isolates of *S. pneumoniae*. Such isolated should also be tested against vancomycin using the MIC or disk method. With isolates form other sites, the oxacillin disk screening test may be used. If the oxacillin zone size is ≤19mm, penicillin and cefotaxime or ceftriaxone or meropenem MICs should be determined.

l. ***Rx*:** Rifampin should not be used alone for antimicrobial therapy.

Streptococcus spp.

m. **Rx:** Penicillin- or ampicillin-intermediate isolates mat require combined therapy with an aminoglycoside for bactericidal action.

n. Not routinely reported on organisms isolated form the urinary tract.

o. Susceptibility testing of penicillins and other beta-lactams approved by FDA for treatment of *Streptococcus pyogenes* or *Streptococcus agalactiae* is not necessary for clinical purposes and need not be done routinely, since as with vancomycin, resistant strains have not been recognized. Interpretive criteria are provided for pharmaceutical development, epidemiology or monitoring for emerging resistance. Any strain found to be intermediate or resistant should be referred to a reference laboratory confirmation.

p. Report against *S. pyogenes*.

q. ***Rx*:** Recommendations for intrapartum prophylaxis for Group B streptococci are penicillin or ampicillin. While cefazolin is recommended for penicillin-allergic women at low risk for anaphylaxis, those at high risk for anaphylaxis may receive clindamycin or erythromycin. Group B streptococci are susceptible to ampicillin, penicillin, and cefazolin, but may be resistant to clindamycin and/or erythromycin. When a Group B *Streptococcus* is isolated from a pregnant woman with severe penicillin allergy (high risk for anaphylaxis) clindamycin and erythromycin should be tested and reported.

r. For this table, the beta-hemolytic group includes the large-colony-forming pyogenic strains of streptococci with Group A (*S. pyogenes*), C, or G antigens and strains with Group B (*S. agalactiae*) antigen. Small-colony-forming beta-hemolytic strains with Group A, C, F, or G antigens (*S. anginosus*, previously termed "*S. milleri*") are considered part of the viridans group, and interpretive criteria for the viridans group should be used.

REFERENCES

Performance Standards for Antimicrobial Susceptibility Testing; Informational Supplement, M100. 2009. Clinical Laboratory Standards Institute (CLSI - formerly NCCLS), Wayne, PA.

For more information, please consult the most current CLSI document.

013009nm

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